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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,089	08/21/2003	Marcel Behr	STAN-102CON2	1719

24353 7590 11/18/2004

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/647,089	BEHR ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2003*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

A. 1-16. Claims 1-7, 19 & 22-23 drawn to nucleic acids and primers comprising a junction of a deletion marker of Table 1 (RD01-RD16), and nucleic acid-based methods of distinguishing a bacterial strain of the *M. tuberculosis* complex featuring the detection of the absence of the marker sequence using a unique deletion marker junction, classified in class 536, subclass 23.1; class 435, subclass 6.

B. 17-32. Claims 8-10, drawn towards recombinant host cells comprising an exogenous nucleic acid comprising a deletion marker of Table 1 (RD01-RD16); class 435, subclass 252.3.

C. 33-48. Claims 11-15, drawn to a genetically altered mycobacterium comprising a deletion resulting from homologous recombination within a deletion marker as set forth in Table 1 (RD01-RD16), classified in class 435, subclass 253.1.

D. 49-177. Claims 16-18, drawn to methods of determining if a patient has been exposed to *M. tuberculosis*, classified in class 435, subclass 7.1; class 424, subclass 9.1.

E. 178-306. Claims 19 and 21, drawn to antibody methods for distinguishing a bacterial strain of the M. tuberculosis complex, classified in class 435, subclass 7.1.

F. 307-322 Claims 19-20 are drawn to nucleic acid-based methods for distinguishing a bacterial strain of the *M. tuberculosis* complex featuring the detection of the presence of a deletion marker using a nucleic acid that hybridizes to the marker nucleic acid sequence, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

Within each of the larger groupings (A-F), the individual groups are distinct from one another based upon the specific structural/functional characteristics of the deletion marker or open reading frame to which the group is directed. For example, there are 16 different deletion markers described in Table 1 (RD01-RD16) that comprise between them 129 different open reading frames (ORFs) encoding distinct polypeptides. For each grouping where the claims are directed towards a deletion marker or deletion marker junction (i.e. groupings A-C), applicants are required to elect a group comprising a single deletion marker and/or its junction from Table 1. For each grouping where the claims are directed to a single polypeptide (i.e. groupings D & E), applicants are required to elect a group comprising a single ORF. This is not an election of species.

Inventions of Grouping A (i.e. Groups 1-16), Grouping B (i.e. Groups 17-32) and Grouping C (Groups 33-48) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as usable together and have different modes of operation, functions and effects. The methods and compositions of Grouping A are directed towards identifying by

nucleic acid-based methods (e.g. hybridization and/or amplification) whether a particular mycobacterial strain is part of the *M. tuberculosis* complex. The recombinant host cells of Grouping B comprise exogenous DNAs comprising at least a portion of a deletion marker (e.g. an ORF). Such strains are useful, for example, in developing attenuated vaccines against a virulent strain of *Mycobacteria* that naturally comprises the sequences found within the deletion marker. The inventions of Grouping C, on the other hand, are directed to cells that lack at least a portion of a deletion marker as described in Table 1. Thus, the inventions of the three different Groupings are biologically and functionally different and distinct from one another and have different effects.

Inventions of Groupings A-C and Groupings D-F are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as usable together and have different modes of operation, different functions and different effects. The nucleic acid-based methods and compositions of Grouping A are directed towards distinguishing between strains of *Mycobacteria*. The recombinant cells of Groupings B and C are directed towards cells that either comprise exogenous DNA comprising a deletion marker (Grouping B) or towards cells that lack at least part of a deletion marker. The inventions of Groupings D (Groups 49-177) and Grouping E (Groups 178-306) are directed towards immunological methods dependent upon the proteins expressed by ORFs within the deletion markers of Table 1. Thus, the methods and compositions of Groupings A-C (i.e. nucleic acid-based methods and compositions dependent upon the presence or absence of a DNA sequence) are functionally and operationally distinct from those

of Groupings D-E (i.e. immunologically-based methods dependent upon protein-protein interactions). With regard to Groupings A and F, while both groupings are directed to nucleic acid-based methods for distinguishing a bacterial strain of the *M. tuberculosis* complex, one grouping is directed to detection of the presence of a unique deletion marker junction and the other is directed to detection of the presence of the deletion marker sequence itself. As such, the methods of Groupings A and F necessarily comprise different methods steps requiring different components (e.g. a nucleic acid that hybridizes across a deletion marker junction versus a nucleic acid that hybridizes to a sequence found in the deletion marker), and result in different outcomes (i.e. detection of a mycobacterium lacking a deletion marker sequence versus detection of a mycobacterium comprising the deletion marker sequence).

Inventions of Grouping D through F are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as usable together and have different modes of operation, functions and effects. The methods of Grouping D are directed towards an immunologically-based method for determining if a sample obtained from a patient comprises antisera against a polypeptide expressed by an ORF found within one of the deletion markers of Table 1. This involves obtaining a sample from a patient (e.g. blood serum) and testing with a protein to determine if protein-specific antibodies are present. The methods of Grouping E do not involve a patient and function in the reverse. In these methods, a sample comprising *Mycobacteria* is tested with protein-specific antibodies to determine if the sample comprises a particular protein. In one case, the methods result in determining if a patient has been exposed to

a particular mycobacterium. In the other case, the methods result in distinguishing between strains of the *M. tuberculosis* complex. The methods of Grouping F are directed to a nucleic acid-based method for distinguishing a member of the *M. tuberculosis* complex . As such, the methods of Grouping F comprise methods steps that are not present in, or required for, the methods of Groupings D or E. Thus, the methods of the three Groupings are biologically and functionally different and distinct from one another, and have different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. In addition, the nonpatent literature search required for the different groups is not coextensive for each group (e.g. nucleic acid-based methodologies versus immunologically based methodologies; PCR methods versus hybridization methods; use of deletion marker junctions versus deletion marker sequences themselves). Finally, with regard to the restriction between different nucleic acid sequences (i.e. deletion marker junctions, deletion markers and/or open reading frames), each individual sequence requires a different search of the sequence databases and places an undue burden on the office if a search of multiple, unrelated sequence searches are required in order to determine patentability for an elected invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

ggl

GERRY LEFFERS
PRIMARY EXAMINER